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Achieving Physiologic Perfusion with Ventricular Assist Devices: Comparison of Control Strategies

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Abstract— **Rotary blood pumps (RBP) are currently being used as a bridge to transplantation as well as for myocardial recovery and destination therapy for patients with heart failure. Physiologic control systems for RBP that can automatically and autonomously adjust the pump flow to match the physiologic requirement of the patient while avoiding suction for varying clinical and physical activity conditions are needed to reduce human intervention and error, and to improve the quality of life. For RBP used as left ventricular assist devices (LVAD), we hypothesize that maintaining a constant average pressure difference between the pulmonary vein and the aorta (ΔPa) or maintaining a constant average pressure difference between the left ventricle and the aorta (ΔP) would give rise to a physiologically adequate perfusion while avoiding LV suction. Using a mock circulatory system we tested the performance of the control strategy of maintaining a constant average ΔPa and a constant average pump pressure head (ΔP) and compared it with the results obtained when constant rpm is maintained. The comparison was made for normal, failing, and asystolic left heart during rest and at light exercise. The ΔPa was maintained at 95 ± 1 mmHg and ΔP was maintained at 75 ± 1 mmHg for all the scenarios. The results indicate that the ΔPa control strategy maintained or restored the total flow rate to that of the physiologically normal heart during rest (3.8 l/m) and light exercise (5.4 l/m) conditions. The ΔPa approach adapted to changing exercise and clinical conditions better than the constant rpm and constant ΔP control strategies. Our computer simulation studies indicate that the ΔP control strategy performs better than the constant rpm control strategy, especially at higher cardiac demand situations, which could not be tested experimentally due to the limitation of the mock circulatory system.**

INTRODUCTION

Ventricular assist devices have been used successfully for many years as a bridge to transplantation and hold the potential to become a long-term alternative to donor heart transplantation (destination therapy). However, a control system that automatically responds to physiological cardiac demand for continuous flow ventricular assist devices (VADs) does not exist.

Several physiological indicators of cardiac demand like atrial pressure, blood oxygen saturation, lactic acid concentration in blood, P wave activity of the atria, renal sympathetic nerve activity and aortic nerve activity have been identified. However, these physiological indicators are influenced by factors other than cardiac demand, and lack accurate and sensitive sensors to measure them reliably over long term [1]. Additionally, physiologic indicators, which current control strategies (both in literature and in practice) rely upon, *change* with variation in cardiac demand. For example, if the control objective is to maintain a reference VAD rpm, an increase in cardiac demand would necessitate an increase in the desired rpm according to some expert rule, or model prediction. In contrast, the average pressure difference between pulmonary vein and aorta (ΔPa) or the average pressure difference between the left ventricle and the aorta (ΔP) are almost constant for varying levels of cardiac demand, does not decay with time and can be reliably measured. Hence, we suggest that *maintaining an average reference ΔPa or ΔP is an appropriate strategy for controlling ventricular assist devices*. The natural regulatory system varies the vascular resistances to maintain the required flow of blood [2], [3] with an almost constant average ΔPa or ΔP. By using a VAD to assist the failing heart in maintaining the prescribed average ΔPa or ΔP we, in effect, synchronize the assist and natural perfusion, thus indirectly incorporating natural cardiovascular regulation into the VAD control.

In this paper, the hypotheses of maintaining a constant average ΔPa and ΔP to achieve physiologically motivated perfusion are tested for a centrifugal blood pump using an in-vitro mock circulatory system [4] for the following test conditions: normal, failing, and asystolic left heart during rest and light exercise. Computer simulation studies are used to compare the performance of the ΔP and constant rpm control strategies at higher cardiac demand conditions.

METHODS

Experimental Design

In-vitro testing: An adult mock circulation [4], [5] (consisting of a mock left ventricle, ventricular apical inflow cannulation and mock systemic vasculature with aortic root outflow cannulation) along with a centrifugal flow continuous blood pump (BioMedicus, Medtronic, Eden Prairie, MN) was used to test the viability of the ΔPa control strategy and compare it to constant rpm and constant pump pressure head control strategies, Figure 1.

To study the range of applicability of the proposed approach, one normal and two different pathological cases of the VAD-assisted perfusion were simulated using the mock circulatory system. In the first case, the left ventricular assist device (LVAD) was attached to the human equivalence

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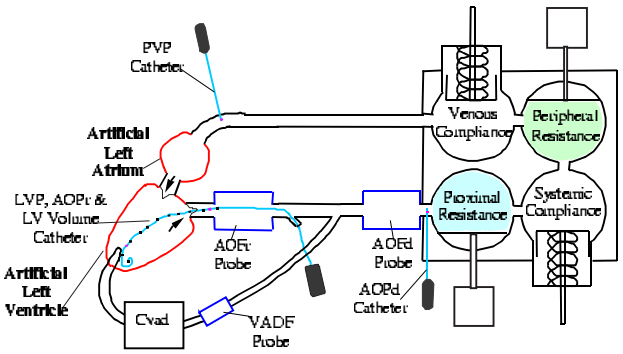

Fig. 1. Schematic of the mock circulatory system with the assist device

of a normal healthy heart, which is a realistic case when testing with animals, or when natural left heart (LH) function has completely recovered after VAD implantation, as observed in several clinical cases [6]. Human equivalence of pathological cases include LVAD assistance of failing and asystolic left heart [5]. All three scenarios were tested under rest and light exercise conditions. Heart rate was 60 bpm during rest and 100 bpm during light exercise. For all test conditions, 35% systole and 65% diastole was maintained. A lower value of heart rate, and the resulting lower cardiac output during rest were chosen to increase the variability in the cardiac demand as the maximum flow rate of the mock circulatory system is limited. The aortic input impedance and vascular mechanical properties were controlled to simulate the flow and impedance of the normal human vasculature [7]. The vascular resistance (total peripheral resistance) and the driveline pressure (which controls the contractility of the LV) were adjusted to match the pressure and flow waveform characteristics of the human circulatory system under the described scenarios. Once the resistance and the driveline pressure is determined, it is used consistently to test different control strategies.

For different clinical and cardiac demand conditions, the VAD rpm is adjusted manually until the setpoint for ΔPa, ΔP or rpm is reached. The setpoint for ΔPa is selected as the ΔPa value observed with normal unassisted heart (baseline case) at rest and is equal to approximately 95 mmHg. Based on the result of the previous simulation study [8], the setpoint for ΔP is selected as 75 mmHg. The pump speed of approximately 1440 rpm, which was needed to restore the cardiac output to the physiologic level of 3.8 l/m for the case of failing heart at rest, is selected as the rpm setpoint. Once the setpoint is reached, the limit cycle hemodynamic waveforms were recorded at 400 Hz with and without VAD assistance for each of the three control strategies. Characterizing hemodynamic parameters, waveform morphology, and ventricular pressure-volume loop responses were calculated to identify differences in the performance with different control strategies for each test condition.

Computer Simulation: The maximum flow rates and cardiac demand conditions that could be simulated using a mock circulatory system was limited to about 6 lpm due to limitations of the mock. A dynamic computer model of an axial and centrifugal flow pumps were developed and incorporated into a computer model of the cardiovascular system [1], [8] to test the control strategies at higher cardiac demand scenarios. The ΔP control approach was compared to a constant rpm control strategy for a normal, failing and asystolic LV during rest, light exercise and strenuous exercise conditions. The native heart rate was 60 bpm during rest, 90 bpm during light exercise and 135 bpm during strenuous exercise. The pump speed of approximately 1435 rpm for the centrifugal pump, and 9749 rpm for the axial flow pump which were needed to restore the cardiac output to the physiologic level of 4.9 l/m for the case of failing heart at rest, were selected as the rpm setpoints for the respective pumps. Once the setpoint is reached, the limit cycle hemodynamic waveforms were recorded with and without VAD assistance for each of the three control strategies. Characterizing hemodynamic parameters, waveform morphology, and ventricular pressure-volume loop responses were calculated to identify differences in the performance with different control strategies for each test condition. All test cases were simulated for 300 cardiac cycles and the limit cycle values for each parameter were averaged to give a single representative value.

RESULTS

Mock circulatory system:

The hemodynamic parameters for a normal, failing and asystolic LV with and without continuous assist for each of the three control strategies during rest and light exercise are listed in Table I, where Case 1 is normal LV at rest; Case 2: Failing LV, rest; Case 3: Asystolic LV, rest; Case 4: Normal LV, exercise; Case 5: Failing LV, exercise; Case 6: Asystolic LV, exercise.

Without VAD assistance, the values of the total flow rate, ΔP and ΔPa decrease during ventricular failure at rest and exercise in comparison to the normal LV at rest and exercise. The left ventricular end diastolic pressure for all the control strategies remain within 3 mmHg of the baseline normal LV value. Since the left ventricular pressure and volume sensor is introduced through the aortic valve (Figure 1), there is a back flow through that valve for baseline and all VAD assist scenarios.

Table I indicates that all the tested control strategies increase the total flow, ΔP and ΔPa with failing and asystolic LV. The ΔPa control strategy maintains or restores the total flow rate to that of the physiologically normal heart during rest and exercise, and adapts best to the need for support. For example, in the case of the normal heart during rest and exercise, the average net VAD flow rate with this strategy is close to zero, as expected, since the native LV provides all the required cardiac output.

TABLE I

COMPARISON OF ASSISTED AND UNASSISTED PERFUSION UNDER DIFFERENT SCENARIOS

Case	VAD rate (rpm)	Total flow (l/m)	ΔP (mmHg)	ΔPa (mmHg)	VAD flow (l/m)	LVPed (mmHg)
BASELINE VALUES						
1	0	3.8	54.3	94.4	0.0	0.0
2	0	2.0	30.5	51.5	0.0	17.2
3	0	0	–	–	–	–
4	0	5.4	54.4	98.4	0.0	-6.7
5	0	3.1	32.9	58.7	0.0	16.4
6	0	0	–	–	–	–
CENTRIFUGAL VAD WITH ΔPa CONTROL						
1	800	3.6	55.3	95.0	0.2	1.0
2	1440	3.9	71.9	95.2	4.5	-0.8
3	1490	3.9	96.4	94.9	4.5	-1
4	650	5.5	51.7	95.8	-0.4	-5.3
5	1490	5.2	68.6	94.4	5.6	-5.1
6	1600	5.7	98.3	95.2	6.3	-2.8
CENTRIFUGAL VAD WITH ΔP CONTROL						
1	1300	4.6	75.3	115.4	3.2	-1.3
2	1450	4.0	78.2	101.2	4.5	-1.3
3	1320	3.3	75.6	74.5	3.9	0.0
4	1280	6.4	74.6	117.5	3.5	-7.6
5	1600	5.7	76.6	101.5	6.2	-6.2
6	1400	4.8	74.1	71.6	5.4	-0.1
CENTRIFUGAL VAD WITH RPM CONTROL						
1	1450	4.7	80.1	120.2	3.8	-1.8
2	1440	3.9	71.9	95.2	4.5	-0.8
3	1450	3.7	89.3	87.8	4.3	-1
4	1440	6.8	80.0	122.4	4.4	-7.9
5	1440	4.8	70.5	97.0	5.3	-4.8
6	1440	5.0	76.6	74.0	5.5	-0.6

Figure 2 shows the comparison between the total flow rates (sum of VAD flow rate and cardiac output) at baseline and during assistance using constant rpm, ΔP and ΔPa control strategies during rest and exercise scenarios for each clinical test condition. The baseline cardiac output of 3.8 l/m at rest and 5.4 l/m during light exercise are considered to be physiological flows for the corresponding physical activities. The comparison of total flow rates produced with different control strategies shows that the ΔPa approach best matched the physiologic flow rate. The comparison of rest and exercise cases shows that the control strategy of maintaining an average ΔPa leads to the correct adaptation to changing cardiac demand. For a normal LV, the ΔPa control strategy best matches the physiologic flow rates, Figure 2a. At the same time, the constant rpm and ΔP control strategies result in higher than normal flow rate. The overpumping (highest when constant rpm is maintained) increases the risk of LV suction.

Figure 2b indicates that when the failing LV is assisted by a VAD, all three control strategies restore the total cardiac output to near physiologic level. The ΔPa approach best matches the physiologic flow rate during rest and exercise. The ΔP approach leads to an output that is slightly higher than the physiologic flow rate. The constant rpm strategy results in a lower than normal flow rate during exercise, increasing the chances of under perfusion during higher cardiac demand.

With an asystolic LV (Figure 2c), the ΔPa strategy is the best approach at restoring the flow rates to near physiologic values, followed by constant rpm and ΔP strategies. Overall, the ΔPa strategy consistently produced a total flow rate that is the closest to the physiological flow rate for all heart conditions and physical activity scenarios.

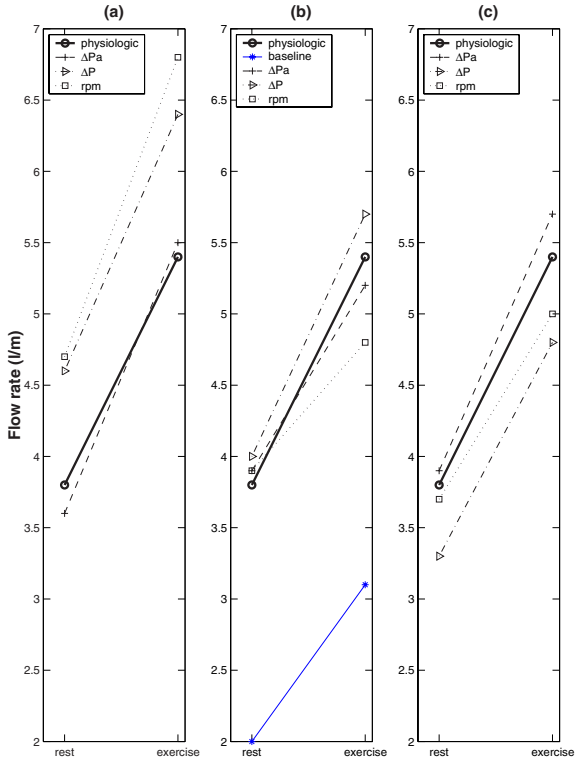

Fig. 2. Comparison of total flow generated with ΔPa, ΔP and constant rpm strategies with and without the VAD: (a) Normal LV; (b) Failing LV; (c) Asystolic LV;

The left ventricular pressure-volume relationships for a normal and failing LV with and without assistance is shown in Figure 3. All the tested control strategies cause a leftward shift in the pressure volume loop for a failing ventricle during rest and exercise, Figure 3c&d, and a lowering of left ventricular end diastolic pressure, indicating a correct direction of adaptation for all the control strategies. Except for the result with ΔPa control, a leftward shift in the PV loop and lowering of LVPed was noticed for a normal heart assisted by a VAD during rest and exercise (Figure 3a&b), indicating an increased likelihood for suction.

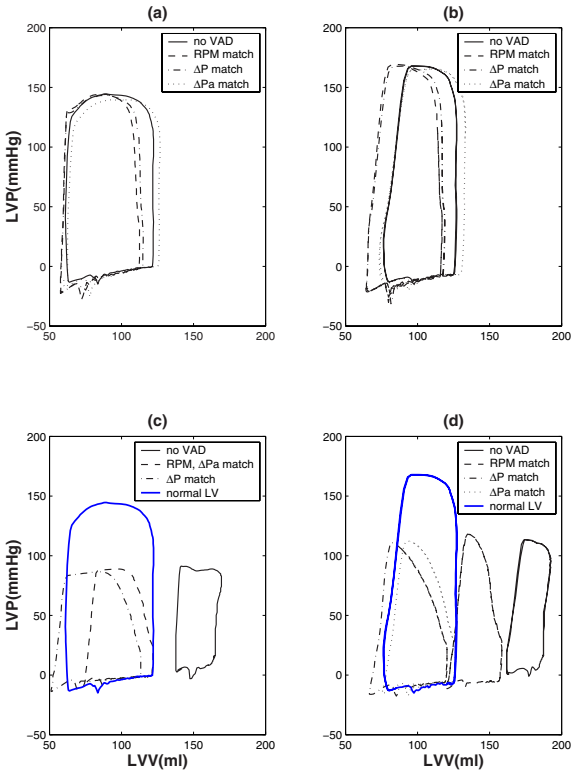

Fig. 3. PV loops with and without VAD assistance using constant rpm, ΔP and ΔPa control strategies for the following test conditions: (a) Normal LV during rest; (b) Normal LV during exercise; (c) Failing LV during rest; (d) Failing LV during exercise.

Computer Simulation:

Table II summarizes the simulation results and compares cardiac output, AoP, LVEDP and LH volume for all studied cases[1]. The cases listed in Table II are as follows: Case 1 is for normal LV at rest; Case 2: Failing LV, rest; Case 3: Asystolic LV, rest; Case 4: Normal LV, light exercise; Case 5: Failing LV, light exercise; Case 6: Asystolic LV, light exercise; Case 7: Normal LV, heavy exercise; Case 8: Failing LV, heavy exercise; Case 9: Asystolic LV, heavy exercise. In all cases, the VAD assistance reduces the LVEDP and increases the cardiac output to near normal values. It can also be noted that for both pumps, though vastly different in their characteristics, the proposed control strategy leads to an adequate overall perfusion, and produce strikingly similar results for different pathological conditions and varying levels of physical activity. The overall conclusion of the simulation study is that maintaining an average reference ΔP results in physiological perfusion irrespective of the type of pump used, and is both physiologically motivated and sound. The comparison of rest and exercise cases shows that the proposed control strategy leads to a correct adaptation to the changing cardiac demand.

The adaptation of the proposed control strategy to the changing exercise and clinical conditions was then compared with the adaptability obtained with the traditional VAD controller, designed to maintain a constant pump rpm. Constant rpm setpoints of 9749 rpm and 1435 rpm were selected for the axial flow and centrifugal pumps respectively, which were the average pump speeds observed with the designed ΔP controllers during rest. When a constant rpm is maintained and the physical activity is transitioned to heavy exercise, the volume of the weakened LH with VAD support reduces from 221/303 ml, observed without VAD assistance to approximately 175/219 ml with the axial flow pump and 197.6/249.8 ml with the centrifugal pump. These values are still higher than the normal range, though the adaptation is in the right direction. The RH pressure does not reduce significantly and is above the normal range, and is only marginally better than without a VAD. The cardiac output is 11.88 lpm with the axial flow VAD and 11.48 with the centrifugal VAD, which is substantially less than normal 14.62 lpm observed with the normal heart during heavy exercise. The difference in adaptability of the constant ΔP and constant rpm control strategies is less pronounced during a more likely clinical scenario of light exercise, though the proposed approach still results in the total cardiac output closer to the normal value.

DISCUSSION

The importance of adequate VAD control cannot be overstated. Though the design of the VAD itself is critical to the long-term success of the electro-mechanical implant, the control of the VAD determines the confidence of doctors and patients in the VAD as a permanent solution and an alternative to donor heart transplantation. The key requirement of the automatic control system is the adaptation of VAD-generated flow to the changing physiological requirements of the patient while reliably avoiding suction [9], [10], [11].

Our in-vitro results show that maintaining a constant average ΔPa or ΔP is an effective way to the correct adaptation of the cardiac output to changing requirements of the patient irrespective of the type of rotary pump used to assist perfusion. The physiological explanation of this conclusion rests with the fact that the vascular bed resistance can increase or decrease by a factor of 2 to 5 [12] in response to the changing cardiac demand and is the dominant factor in regulating perfusion. The blood flow is inversely proportional to the vascular bed resistance so that maintaining a constant ΔPa or ΔP with changing resistance can increase or decrease the flow rate by the same factor of 2 to 5.

The desired (reference) ΔPa or ΔP can be maintained by adjusting the pump rpm within physiologically admissible limits despite the changing vascular resistance, stroke volume and heart rate, which represent the response of

[1]It should be noted that without ventricular assistance a person with profound heart failure cannot perform strenuous exercise. Therefore, the simulation results corresponding to failing heart during exercise without VAD assistance should be viewed as an idealization used for comparison with the VAD-assisted case.

TABLE II

COMPARISON OF ASSISTED AND UNASSISTED PERFORMANCE OF THE CIRCULATORY SYSTEM UNDER DIFFERENT SCENARIOS

	Total Output (lpm)	AoP (mmHg)	LVEDP (mmHg)	LH Volume (ml)
NO VAD ASSISTANCE				
1	4.92	125/80	1	77/159
2	3.6	95/59	25	215/275
3	0	–	–	–
4	7.98	126.8/76.7	1	77.7/166.4
5	6.19	97.6/58	27.3	218.9/287.6
6	0	–	–	–
7	14.62	131/71	1	80/190
8	11.07	100/50	28	221/303
9	0	–	–	–
AXIAL FLOW VAD, ΔP CONTROL				
1	4.98	121/89	0.7	39/107
2	4.56	99/91	11	82/119
3	4.32	89.7	14.7	147
4	8.13	114.8/95.4	0.6	39.6/94
5	7.36	97.5/92	11.2	82.4/117.7
6	7.02	89.6	14.6	146
7	14.85	109/98	0.5	40/90
8	13.65	95/92	11	79/117
9	12.92	89.4	14.4	144
AXIAL FLOW VAD, CONSTANT 9749 RPM CONTROL				
5	6.96	95.1/84.4	15.2	121.3/159.9
8	11.88	87/76	21	175/219
CENTRIFUGAL VAD, ΔP CONTROL				
1	5.0	105/101.7	0.6	52/78.7
2	4.54	94.7/93.6	11	89.6/116
3	4.32	89.6	14.6	146
4	8.12	104.1/102.2	0.6	51/80
5	7.40	94.2/93.6	11	87.1/115.3
6	7.02	89.6	14.6	146
7	14.85	102.9/102.4	0.5	83.6/48
8	13.64	93.7/93.5	11	82/116.4
9	12.92	89.5	14.5	145
CENTRIFUGAL VAD, CONSTANT 1435 RPM CONTROL				
5	6.52	84.2/81.8	19.9	209/180.7
8	11.48	90.9/69.5	23.7	197.6/249.8

the natural regulatory mechanisms to the changing physiological cardiac output demand. The dominant role of the changing resistance in adaptation to physiological demand [2], [3] implies that by maintaining, on average, the prescribed ΔPa or ΔP we, in effect, synchronize the assist and natural perfusion, thus indirectly incorporating natural cardiovascular regulation into VAD control.

The proposed approach to the control of RBP requires that the natural regulatory mechanism functions properly in response to changing cardiac demand, which may not always be the case. For example, medical intervention may be necessary in the case of severe hypertension (often seen in the VAD recipients after initial recovery), which could lead to higher than normal arterial pressures, resulting in lung edema. Note that neither the alternative VAD control strategies, nor the natural heart can directly mitigate arterial hypertension, and the resulting lung edema. Consequently, the long-term goal may have to include the development of an automatic, autonomous and portable health monitoring and management system for patients with the permanent VAD or TAH, which would combine real time control of the blood pump with the automatic monitoring of the cardiac function, and, if necessary, emergency drug administration, and other advanced functionalities.

The primary advantage of the ΔPa control strategy is its ability to autonomously adjust the total output, defined as the sum of cardiac and pump outputs, to match the cardiac demand better than any alternative strategies. ΔPa, being the difference between the aortic and the pulmonary venous pressure (equal to left atrial pressure), is sensitive to changes both in preload and afterload.

The current in-vitro study shows that the proposed strategy of maintaining the desired average ΔPa leads to an adequate adaptation for widely changing cardiac demand and clinical conditions in a completely autonomous way. The results show that, though some degree of physiological adaptation is achieved with constant rpm and constant ΔP, these alternatives are less effective for a wide range of physical activities, and rapidly changing status of cardiac function (such as a sudden transition from failing to asystolic heart). With the constant rpm control strategy, broad range of physical and clinical conditions would require an external intervention to change the rpm setpoint according to some expert rule, model prediction or operator input. The constant ΔP approach does not perform as well as the ΔPa approach for a broad range of clinical conditions of the native heart, which changed from normal to asystolic LV in this study, but adapts well to the changing cardiac demand due to different exercise levels. The in-vitro study is consistent with the results of computer simulations, which shows that the ΔP control strategy adapts better to widely varying cardiac output requirements when compared to the traditional constant rpm control approach. Due to the limitations of the mock circulatory system, we were unable to test the higher cardiac demand conditions to make an in-vitro comparison between the different control strategies. Higher cardiac demand conditions were tested using computer simulations.

In the limited range of cardiac demands that could be tested in-vitro, the performance of the ΔPa control strategy is superior to ΔP and constant rpm control alternatives. Using the proposed approach, both the natural heart and the assist device are contributing to the pumping action of maintaining an average ΔPa. If cardiac function improves, the native heart will increase its contribution to maintaining the reference pressure difference, with the VAD controller autonomously and automatically responding to

the decreased need for assisted perfusion, as evidenced by the near zero net VAD flow rate with the normal heart during rest and exercise. When the net flow rate through the VAD is close to zero, blood does not stagnate inside the VAD, though the residence time of blood in the pump is higher, increasing the probability of hemolysis. Since this scenario occurs only with a normal or near normal heart, the patient could be weaned from the pump at this stage.

The ability of the proposed control strategy to automatically adjust its contribution towards maintaining ΔPa may prove to be well suited to the application of the ventricular assist devices in cardiac recovery therapy [6], [13] of end stage heart failure (alone or in combination therapy), as well as in the destination therapy.

Though not directly addressed in this paper, the overarching principle behind the proposed approach of maintaining key pressure differences with mechanical blood pumps, while relying on the natural regulation to adjust the resistances to the blood flow to meet the physiological demand is also applicable to the case of pulsatile ventricular assist devices, as well as the total artificial heart. In the case of the TAH, the blood pump should be controlled to maintain key pressure differences at the average reference values, which, in the case of pulmonary circulation, is the difference between pulmonary arterial and vena cava pressures.

In its current form, for the case of VAD control the proposed approach requires two pressure sensors, which may not be clinically feasible for long term implantation. However, for different types of blood pumps, it may be possible to estimate ΔPa and ΔP using the pump model, and only intrinsic and readily measurable pump parameters (such as pump rpm, voltage and current), eliminating the need for implantable pressure sensors. The approach which utilizes a blood pump as both the actuator and the flow or pressure sensor, can be viewed as a "sensorless" control [14]. Sensorless estimation of ΔPa and ΔP is currently being pursued as a follow-up investigation.

CONCLUSION

The presented in vitro results show that maintaining an average pressure difference between the pulmonary vein and aorta (ΔPa) provides an effective way to control a continuous flow LVAD over a wide range of physiological and cardiac demand conditions while maintaining an average pressure difference between the left ventricle and aorta (ΔP) provides an effective way to control a continuous flow LVAD over a wide range of cardiac demand conditions for the same cardiac condition. Both strategies reduce the probability of suction. Change in vascular resistance is the dominant regulatory mechanism in meeting the physiological requirements for blood perfusion. Maintaining the desired average ΔPa or ΔP by adjusting the pump rpm during changing cardiac demand, in effect, synchronizes the assist and natural perfusion. Therefore, the proposed control strategies indirectly incorporates natural cardiovascular regulation, which changes vascular resistance, into VAD control. The comparison with the VAD control systems, which maintain either constant reference pump rpm, or constant pump pressure head (ΔP) shows that the ΔPa approach is superior in autonomously maintaining an adequate perfusion during changing cardiac demand for the test conditions simulated in vitro. Since the ΔPa control strategy automatically adjusts its contribution to the total flow based on the function of the native ventricle, the proposed approach may prove to be well suited to the application of the ventricular assist devices in recovery therapy.

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